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Original Article: Clinical Investigation

Systemic inflammatory response syndrome after percutaneous nephrolithotomy: An assessment of risk factors

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Objectives: To analyze the risk factors for systemic inflammatory response syndrome (SIRS) after percutaneous nephrolithotomy (PCNL) and to quantitatively predict the probability of SIRS after PCNL.

Methods: Medical records on 209 patients who underwent PCNL were retrospectively analyzed. The χ^2 test, the *t*-test and a logistic regression model were used to identify key risk factors of SIRS after PCNL. A predictive equation was then formulated to assess the risk of SIRS according to the results from the logistic model. Subsequently, the accuracy of the equation by calculating sensitivity, specificity, overall correct percentage, and positive and negative predictive values was tested.

Results: The incidence of SIRS after PCNL was 23.4%. The key risk factors for SIRS following PCNL were: the number of tracts, receipt of a blood transfusion, stone size, and presence of pyelocaliectasis. Other factors added no independent risk to the development of SIRS. The calculated values for sensitivity, specificity, overall percentage correct, positive predictive value and negative predictive value were 44.9%, 95.0%, 83.3%, 73.3%, and 84.9%, respectively.

Conclusions: Number of tracts, receipt of a blood transfusion, stone size and presence of pyelocaliectasis are identified as the key risk factors for SIRS after PCNL. The predictive equation allows for an individualized and quantitative assessment of the probability of SIRS after PCNL.

Key words: assessing, kidney calculi, percutaneous nephrolithotomy, risk factors, systemic inflammatory response syndrome.

Introduction

Percutaneous nephrolithotomy (PCNL) has been one of the most important procedures for handling stones in the upper urinary tract. However, temporary urosepsis is a potential catastrophic complication following PCNL.[1] Mild sepsis or fever may be attributed to postoperative bacteremia. The patients involved are hemodynamically stable and do not have a longer hospital stay than others receiving the procedure.[2] However, patients with complicated stones may develop postoperative systemic inflammatory response syndrome (SIRS), and some of these patients even progress to multiple organ dysfunction syndrome (MODS). When MODS occurs, even intense supportive treatment has made little impact on the mortality rate over the past 20 years.[3] Therefore, an investigative basis should be established for the prevention and treatment of SIRS.

SIRS mainly occurs in patients with polytrauma or severe burns, or in those who have undergone a major operation.[4] A variety of causes may be involved in the initiation of SIRS, including hypoxia, enhanced adrenergic activity, or changes in blood flow.[5,6] Researchers have attempted to detect influencing factors for the development of SIRS, such as the creation of second tracts, an operative time >90 min,[7] a blood transfusion in the first 24 h after trauma,[8] a pelvic urine culture,[9] and preoperative antibiotics.[10] However, neither the pathophysiological mechanism of SIRS[11] nor the key causes for SIRS after PCNL are currently known. In this study, we added four more factors as possible causes, namely stone size, presence of pyelocaliectasis, stone configuration, and pyonephrosis. According to our experience, these additional factors are suspected to be causes and were added in order to clearly present the relationship between the eight factors and SIRS after PCNL. They were also added to provide an individualized assessment of the risks for SIRS after PCNL.

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Methods

In this study, we retrospectively analyzed the clinical data of 209 consecutive patients who underwent PCNL at the Department of Urology, Peking University People's Hospital, from January 2005 to February 2007. This study was approved by the Institutional Ethic Committee of Peking University People's Hospital. All participants provided written informed consent.

The exclusion criteria included: patients with tumors, hematopathy, diabetes mellitus, those taking oral immunosuppressants, patients with a horseshoe kidney, polycystic kidney or ureteropelvic junction stricture, those having a heart rate greater than 90 beats/min before surgery, those with heart or kidney failure, preoperative fever treated with antibiotics, those having a tubeless PCNL, a second PCNL, a minimally invasive PCNL (18-Fr sheath), or a PCNL in combination with another manipulation in one operation.

Preoperative preparation included an ultrasound and a complete blood count. All patients took ciprofloxacin 250 mg twice daily for one week before the PCNL procedure. At the time of induction for the PCNL, all patients received ceftriaxone 2.0 g intravenously if they were not allergic to penicillin. The administration of ciprofloxacin or ceftriaxone intravenously was provided for at least three days after the PCNL to prevent a general infection. In order to differentiate the results of a midstream urine culture and a drug sensitivity screen, a 'low-grade' bacteriuria was defined as growth of a single organism with a colony count of less than 10^5/mL; and 'high-grade' bacteriuria as growth of ≥2 kinds of organisms or any organism with a colony count greater than or equal to 10^5/mL. A dilated pelvis or calices with a maximum diameter more than 10 mm is considered to be pyelocaliectasis in our hospital. Operative time was recorded as from the beginning of puncture to the end of placing an indwelling nephrostomy tube. No matter which side the renal stone was on, operations creating only one tract were regarded

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as single tract operations, and operations creating two or more tracts were regarded as multiple tract operations. The stone was measured at its maximum diameter. Upper urinary tract stones that involved the renal pelvis and extended into at least two calyces are classified as staghorn calculi. SIRS was diagnosed in patients who met two or more of the following four criteria:[4] (i) body temperature lower than 36°C or higher than 38°C; (ii) heart rate greater than 90 beats/min; (iii) respiratory rate greater than 20 breaths/min or PaCO2 less than 4.3 kPa; and (iv) white blood cell count (WBC) greater than 12×109/L or less than 4×109/L.

Patients were placed in the prone position after epidural anesthesia was completed. After routine antiseptic preparation, the percutaneous tract was located at the 11th intercostal space or 12th subcostal site under ultrasonic guidance with an 18-gauge needle. Dilatation of the nephrostomy tract was performed with Alken type metal dilators until a 24-Fr Amplatz sheath was inserted. A 20.8-Fr rigid nephroscope (Richard Wolf, Knittlingen, Germany) was used in combination with ultrasonic and pneumatic lithotripsy (Swiss LithoClast, EMS, Nyon, Switzerland) for stone disintegration in all cases. A 6-Fr or 7-Fr double-J catheter and a 14-Fr nephrostomy tube (BD Medical System, Franklin Lakes, New Jersey, USA) were placed at the end of each procedure. After the PCNL, the patient's vital signs were closely monitored for 24 h and a fasting peripheral blood routine was checked to help with the diagnosis of SIRS the next morning.

In the statistical analysis, the Independent-Samples *t*-test, Pearson χ^2 test and Continuity Correction test were used to analyze the normally distributed data. The Mann–Whitney *U*-test and Spearman correlation test were used for the skewed data. The relative risk (odds ratio, OR) was used in a multivariable logistic regression analysis (Backward: Wald method) to find the key risk factors for the development of SIRS after PCNL. According to the results of the logistic model, a predictive equation was formulated to assess the risk of SIRS. Finally, we tested the accuracy of the equation by calculating the sensitivity, specificity, overall correct percentage, positive predictive value (PPV) and negative predictive value (NPV). We performed all statistical analyses using the SPSS statistical software package (Version 15.0 for Windows, SPSS, Inc). All statistical tests were 2-sided at the 0.05 level or $P < \alpha$ ($\alpha = 0.10$) in the logistic regression analysis.

Results

A total of 209 patients were recruited based on our selection criteria. Table 1 lists the demographic characteristics of the patients and their stones. The mean age was 49.05 years (ranging from 17 to 79), and 132 (63.2%) of the patients were male. Thirteen patients (6.2%) required blood transfusions and no one was involved in a pelvis, colon or pleura perforation. Forty-nine patients (23.4%) developed SIRS after the PCNL. Most (46/49) of the SIRS patients recovered, but three patients developed septic shock and one progressed to MODS (renal dysfunction and type I respiratory failure). Fortunately, they were rescued by supportive treatment in an intensive care unit.

Overall, 84 patients had urine that was colonized. As depicted in Table 2, the most frequent urine-colonizing pathogens were Gram-negative (53.6%). However, the most common organism was Gram-positive (*Staphylococcus,* 25.0%). Patients who had high-grade bacteriuria were predominantly colonized with Gram-negative pathogens (61.5%). In contrast, patients with low-grade bacteriuria were most frequently colonized with Gram-positive pathogens (68.4%). Of the 84 patients, only four patients had blood samples collected for bacteriological evaluation because their postoperative body temperature was higher than 38.5°C for more than three days. The results indicated that two samples were sterile and the others had pathogens involved. It seemed that the pathogens colonizing the blood were different from those colonizing the urine. Of all 209 renal calculi, 61 samples were ground into a fine powder for component analysis by X-ray diffraction (XRD). Four of seven patients whose calculi were identified as struvite developed SIRS (57.1%). SIRS did not occur in the two hydroxylapatite patients.

The correlation of each risk factor and SIRS is shown in Table 3. In the univariable test analysis we found a significant correlation between SIRS and six factors, namely: operative time ($P < 0.001$), stone size ($P < 0.001$), Pyelocaliectasis ($P = 0.007$), the number of tracts ($P < 0.001$), receipt of a blood transfusion ($P < 0.001$) and presence of staghorn calculi ($P = 0.001$). No significant difference was observed in the preoperative urine culture ($P = 0.152$), or for the presence of pyonephrosis ($P = 0.299$) in both SIRS and non-SIRS patients.

In the multivariable logistic analysis, the key risk factors for the development of SIRS after PCNL were: the number of tracts (OR = 24.13, 95% confidence interval [CI] = 4.77–122.00, $P < 0.001$),

Table 1 Demographic characteristics of patients and stones

	Whole group
Age (year)	
Range	17–79
Mean ± SD	49.05 ± 13.55
Sex	
Male	132
Female	77
Operative time (min)	
Range	20–310
Quartiles	50, 70, 100†
Stone size (mm)	
Range	8.2–84.2
Quartiles	14.7, 20.0, 27.5†

†quartiles: 25th, 50th, 75th. SD, standard deviation.

Table 2 Specific pathogens of the midstream urine culture

Pathogen	Low-grade	High-grade
Gram-negative		
Escherichia coli	2	18
Proteus	0	7
Pseudomonas	0	5
Acinetobacter	1	3
Klebsiella	0	4
Alcaligenes	1	1
Burkholderia	1	1
Pasteurella	1	0
Gram-positive		
Staphylococcus	10	11
Enterococcus	3	4
Others		
Mixed growth†	0	9
Candida	0	2

†greater than or equal to two kinds of microorganisms.

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Table 3 Correlation of risk factors and systemic inflammatory response syndrome

	SIRS group	Non-SIRS group	*P*
Operative time (min)	132.72†	96.51†	<0.001*
Stone size (mm)	140.16†	94.23†	<0.001*
Urine culture			
(+):(–)	24:25	60:100	0.152
Pyelocaliectasis			
Yes:No	30:19	63:97	0.007*
Tract			
Single:Multiple	38:11	157:3	<0.001*
Blood transfusion			
Yes:No	11:38	2:158	<0.001*
Pyonephrosis			
Yes:No	4:45	7:153	0.299
Staghorn calculi			
Yes:No	16:33	19:141	0.001*

*$P < 0.05$. †mean rank. SIRS, systemic inflammatory response syndrome.

receipt of a blood transfusion (OR = 22.41, 95% CI = 3.91–128.53, $P < 0.001$), stone size (OR = 1.10, 95% CI = 1.05–1.14, $P < 0.001$), and presence of pyelocaliectasis (OR = 3.35, 95% CI = 1.44–7.81, $P = 0.005$). The other four factors added no independent risk to the development of SIRS. The risk for the development of SIRS was more than 20 times greater when the patient received a blood transfusion or had multiple tracts when compared with the non-transfusion group and the single tract group.

We used the inverse of the logistic function to obtain a predictive equation:

$$P = 1/\left[1 + e^{-(-4.441+3.110\,\text{transfusion}+3.183\,\text{tract}+0.091\,\text{size}+1.209\,\text{pyelocaliectasis})}\right].$$

P was the probability of SIRS after PCNL. According to the logistic rules the critical value was 0.5, which means SIRS occurs at $P > 0.5$. The calculated values for sensitivity, specificity, overall correct percentage, PPV and NPV were 44.9%, 95.0%, 83.3%, 73.3%, and 84.9%, respectively.

Discussion

In our department, percutaneous nephrolithotomy is generally a safe treatment option for handling stones in the upper urinary tract with low complication rates (for instance, blood transfusion rate [6.2%], perforation rate of collecting system and other organs [0.0%]). However, similar to previous reports about the incidence of SIRS after PCNL (25.5%[10] and 22%,[12]) our study found a 23.4% incidence rate regardless of careful preoperative preparation. Probably because most SIRS patients recover without sequelae, some surgeons still ignore the underlying risk of SIRS. It was reported that nine out of 700 (1.3%) patients developed severe sepsis when they underwent percutaneous or endoscopic procedures for upper urinary tract stones, and six of the nine (66%) died.[1] Although in patients who are given intraoperative antibiotics, pyrexia in the immediate postoperative period after PCNL does not mandate an immediate search for bacteremia if the preoperative urine culture is negative.[2] More attention should be paid to this 'micro-invasive' operation and its relationship to postoperative SIRS.

A predictive equation was used as a novel method of describing the probability of SIRS after PCNL. This predictive equation aimed to help patients and doctors predict the probability of SIRS in order to institute a reasonable operation and treatment protocol before PCNL. For example, if a 50 mm stone (at its maximum diameter) has no evidence of pyelocaliectasis, a single tract patient without a blood transfusion would have a 52.7% probability of developing SIRS ($P = 0.527$). This means a similar puncture of a stone smaller than 50 mm would have no SIRS complication ($P < 0.5$). But if the patient has a dilated collecting system, SIRS would occur when the stone size was larger than 35 mm ($P > 0.5$). For this reason, urologists should advise outpatients to undergo a timely PCNL before their stones grow big enough to obstruct the collecting system.

It is possible that few urologists realize that a multiple tract PCNL has a risk of SIRS similar to that of a blood transfusion. Furthermore, a multiple tract patient without pyelocaliectasis would be a SIRS victim if their biggest stone was larger than 15 mm ($P > 0.5$). Since most complicated stones are less than 15 mm at their maximum diameter, multiple tracts (for better disintegration) should be considered cautiously before the PCNL procedure. For normal procedures, a safe, single tract operation is recommended, especially for patients with pyelocaliectasis or elderly patients with chronic diseases. A PCNL needing a blood transfusion often occurs in patients with narrow calyx necks or without caliectasis. If the first difficult tract was closed and a new tract was then created for a better operative field, a 20 mm stone sharply increases the probability of SIRS from 62.0% to 97.5%. In this case, it would be better to stop and wait for a second stage PCNL after the patient recovers.

The reason why staghorn calculi and operative time did not enter the equation as predictive factors was analyzed by multivariable logistic regression analysis and the Spearman correlation test. Operative time (OR = 1.02, 95% CI = 1.01–1.03, $P = 0.001$) and stone size (OR = 1.15, 95% CI = 1.09–1.22, $P < 0.001$) were found to be the key risk factors for staghorn calculi. Furthermore, we found a positive correlation between stone size and operative time (r = 0.277, $P < 0.001$). This is probably because these three factors had such a close relationship; meaning stone size finally entered the equation as a key risk factor behind the other two factors.

Because the equation was deduced only from data in our department, there are inevitable limitations to our study. For example, the predictive equation may not be applicable for young children because there were none enrolled in this study. The high specificity and relatively low sensitivity of the equation may be chiefly due to the poor understanding of the mechanisms of SIRS after PCNL.[11] Many important factors need to be further studied regarding their correlation with SIRS. Furthermore what kinds of factors will ultimately decide whether postoperative SIRS is curable or not? Up to now it has remained a clinical challenge to predict which patients will develop SIRS after PCNL. However, in the same way that the carcinoembryonic antigen (CEA) was not a good predictor in the diagnosis of alimentary tract tumors,[13,14] our equation has warnings that contribute to the incidence of SIRS. We also anticipate that other urologists will test this equation and add other variables to the risk prediction in their own practice.

Conclusions

Our retrospective study demonstrates that the number of tracts, receipt of a blood transfusion, stone size and presence of pyelocaliectasis are key risk factors for the development of SIRS after PCNL. The equation

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allows patients and doctors to predict the probability of SIRS after PCNL in order to institute a reasonable operation and treatment protocol before the PCNL procedure. Urologists should advise their outpatients to undergo a timely PCNL because big stones and pyelocaliectasis will increase the risk of SIRS after PCNL. A multiple tract PCNL for better disintegration should be considered cautiously because of the increased risk of SIRS. We advise the use of our equation during PCNL and recommend that when severe bleeding occurs it is better to stop and wait for a second-time PCNL.

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